REMARKS

Reconsideration of the present application is respectfully requested for the reasons that follow.

Claim Amendments

Claim 22 has been amended to correct an inadvertent typographical error. Claim 22 has also been amended to clarify the nature of the variants of SEQ ID NO:1 and SEQ ID NO:2. There is written description support for this amendment in the specification as filed as shown in paragraph [0007] of the published application. No new matter is added.

Objection to the Claims

The Examiner has objected to claim 22. Specifically, the Examiner notes that "and" should appear between "Fel d 1 chain 1" and "Fel d 1 chain 2." Applicants have amended claim 22 accordingly, as discussed above. Therefore, this objection should be withdrawn.

Claim Rejections under 35 USC § 112, second paragraph

The Examiner has rejected claims 22, 28, 33, 37-38 and 42-47 under 35 USC § 112, second paragraph as being indefinite for the following various reasons.

The Examiner has rejected claim 22 for including a reference to two mutations at amino acid 29 of SEQ ID NO: 1. Specifically, the Examiner argues that it is unclear whether the claim is directed to a variant in which each of these two mutations appear in the alternate, or whether they can both be present at the same time. Applicants disagree with the Examiner's interpretation of the claims. Specifically, claim 22 sets forth a Markush group of variants of SEQ ID NO:1. It is clear from the use of a Markush group that both variants at residue 29 cannot be present in the same variant. However, solely in the interest of expediting prosecution, Applicants have amended the language of claim 22, as discussed above, to clarify that the variants are with respect to the identified SEQ ID NO.

The Examiner has also rejected claim 22 for including a reference to "variants." Specifically, the Examiner notes that claims 22 recites variants of SEQ ID NOs 1 and 2 comprising specified mutations. However, the Examiner argues these variants can read on any polypeptide with the specified mutations even if they have no relation to SEQ ID NOs 1 and 2. Applicants disagree with the Examiner's interpretation of claim 22 and believe that this rejection is an error. First, the variants are claimed with reference to the amino acid of a specific SEQ ID NO and thus cannot include any polypeptide that does not include the amino acid of the specific SEQ ID NO. In addition, the specification only describes the variants with respect to the amino acid sequence of the specified SEQ ID NO (see paragraph [0007] of the published application) and thus cannot encompass any unrelated polypeptide. Furthermore and solely in the interest of

expediting prosecution, Applicants have amended the language of claim 22, as discussed above, to clarify that the variants are with respect to the identified SEQ ID NO, e.g., SEQ ID NO: 1 having Lys29Arg. Therefore, in view of these claim amendments, this rejection of claim 22 and its dependent claims should be withdrawn.

The Examiner has rejected claim 45 for reciting that the fusion protein comprises SEQ ID NO: 4. Claim 45 depends from claim 42 through linking claim 44. The Examiner notes that SEQ ID NO: 4 does not comprise the limitations of claims 42 and 44; specifically, the Examiner argues that SEQ ID NO: 4 does not comprise amino acids added on to the N- and/or C-terminus of the fusion protein. Applicants also believe this rejection is an error. Applicants refer the Examiner to Figure 1, which depicts SEQ ID NO: 4, and to SEQ ID NO: 4 in the sequence listing filed December 9, 2010. Both of these instances clearly show that SEQ ID NO: 4 has a methionine residue on the N-terminus and has the sequence Leu-Glu-$(His)_6$ on the C-terminus. Thus, Applicants believe that claim 45 is correct in its present form, and that this rejection should be withdrawn as to claim 45 and its dependent claims.

Claim Rejections under 35 USC § 112, first paragraph

The Examiner has rejected claims 22, 28, 33, 37-38 and 42-47 under 35 USC § 112, first paragraph, as lacking enablement. Specifically, the Examiner concedes that the specification is enabling for the polypeptides of SEQ ID NOs 1, 2 and 3, as well as

fusions thereof, including SEQ ID NO 4. However, the Examiner argues that the specification does not reasonably provide enablement for the polypeptide variants recited in claim 22. The Examiner reiterates her position that "the claims encompass an enormous number of undisclosed polypeptide variants that may include [a] sequence that is unrelated to ... SEQ ID NO: 1 and 2." It is not clear to Applicants how a claim to a variant of SEQ ID NO: 1, for example, could read on numerous polypeptides that are completely unrelated to SEQ ID NO: 1. The Examiner also argues that claim 22 uses open language and therefore read on "polypeptide variants having any number of mutations in addition to the ones listed in claim 22." Again, Applicants do not understand the Examiner's argument. The mutations that are permissible in the claimed polypeptide variants are specified in two Markush groups in claim 22, and are thus described with closed language ("selected from the group consisting of"). Thus, one of skill in the art would understand that the only mutations that are permissible in the claimed variants are those that are enumerated in the Markush groups. The open language ("comprising") does not modify the enumerated mutations. Thus, an embodiment of claim 22 can be construed (as to SEQ ID NOs 1 and 2) to read on fusion products that comprise SEQ ID NO: 1 or an enumerated variant thereof, together with SEQ ID NO: 2, or an enumerated variant thereof, linked together with a specific peptide linkage. In addition and solely in the interest of expediting prosecution, Applicants have amended the language of claim 22, as discussed above, to clarify that the variants are with respect to the identified SEQ ID NO, e.g., SEQ ID NO: 1 having Lys29Arg. Furthermore, while the open transitional language permits the fusion product to have

polypeptide sequences in addition to the claimed sequences, it does not permit the claimed fusion product to be a polypeptide that is completely unrelated to SEQ ID NOs 1 and 2, nor does it permit mutations in addition to those enumerated in the claims (because of the closed Markush language).

In addition to the issue regarding claim construction, discussed above, Applicants also note that the Examiner states that undue experimentation would be required to provide a pharmaceutical formulation to administer the protein. Applicants traverse.

The Examiner accepts that the skilled person can prepare the heterodimer of the present invention based on the detailed description and examples. Once formed, it would be part of the routine common general knowledge of the skilled person to formulate a protein for administration. In this regard, it should be noted that vaccines for human use have been known for many years prior to the filing of the present application, and techniques for formulating vaccines for injection are well established.

Another common protein-containing pharmaceutical product is based on human or humanized monoclonal antibodies. This is a multi-billion dollar industry and the techniques for formulating the products are well known. Examples include anti-TNF alpha, Omalizumab® (a recombinant DNA-derived humanized IgG1k monoclonal antibody for treating allergic asthma) and Cetuximab® (a chimeric monoclonal antibody for the treatment of certain cancers).

It is not an exaggeration to say that, at the filing date of the present application, all major pharmaceuticals companies world-wide had some focus on products incorporating proteins and the techniques for formulating them were available.

To provide specific examples, a commonplace approach to induce immunogenicity of a protein is to adsorb the protein to carrier substances prior to injection. Aluminum hydroxide, aluminum phosphate or tyrosin are such "classical" carrier substances which are used for vaccines and other proteins in order to induce an immune response after injections. This is a very simple and straight forward approach. Indeed, suitable carriers were commercially available at the filing date of the present application, for example Alhydrogel® from Brenntag, Denmark, which is an aluminum hydroxide carrier specifically intended for protein-containing pharmaceutical formulations. To prepare the formulation, the protein in a buffer (which stabilizes the protein in a refolded state) is simply combined with the carrier. Therefore, the skilled person could prepare a suitable formulation based on his common general knowledge using commercially available materials without an undue burden. Accordingly, this rejection should be withdrawn.

The Examiner has also rejected claims 22, 28, 33, 37-38 and 42-47 under 35 USC § 112, first paragraph, for a lack of written description. This rejection also seems to relate to the claim construction issue discussed above in conjunction with the

enablement rejection. Those claim construction arguments also apply to and obviate this rejection. Accordingly, this rejection should be withdrawn.

Claim Rejections under 35 USC § 102(b)

The Examiner has rejected claims 22 and 37-38 under 35 USC § 102(b) as being anticipated by Gefter (US Patent No. 6,048,962). Gefter is directed to a substantially pure, covalently linked human T cell reactive feline protein isolated from house dust. The Examiner argues that Gefter teaches a Fel d 1 allergen comprising the present SEQ ID NOs 1 and 2, thus anticipating claim 22. Applicants traverse.

Even assuming arguendo that Gefter discloses SEQ ID NOs 1 and 2 of the present application (see SEQ ID NOs 2 and 6, respectively, in US 6,048,962), the Gefter sequences are not brought together and they are certainly not linked with a carbon-nitrogen bond. The claims of the present application are therefore novel over Gefter, at least in view of the peptide linkage limitation of claim 22.

Further, Applicants note that the Gefter disclosure would not render obvious the present claims. It could not have been foreseen that a direct covalent linkage between two subunits in a quaternary structure would have allowed correct folding and functioning of the protein. If the skilled person had considered linking the chains, the default approach would have been to use a linker. Moreover, Gefter simply highlights this fact, since there is no direct link from chain 1 to chain 2 (or vice versa), nor does it even suggest that it would be possible to formulate a functional Fel d 1 protein in this

manner. Instead, Gefter proposed adding an additional number of amino acids which the Applicant has found are unnecessary. It would not have been obvious for the skilled person to link chain 1 to chain 2 directly with any expectation of achieving a functioning product. Moreover, the present approach avoids the use of additional amino acids which could give rise to potential adverse effects.

Since Gefter neither anticipates nor renders obvious the presently rejected claims, Applicants believe that the rejections should be withdrawn, and the claims are in condition for allowance.

In view of the foregoing, it is submitted that the present application is now in condition for allowance. Reconsideration and allowance of the pending claims are requested. The Director is authorized to charge any fees or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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